

I. Amendments

By this amendment, claims 15, 16 and 28 have been amended; and the specification has been amended to delete previously added matter.

This amendment adds no new matter to the specification.

No change of inventorship is necessitated by this amendment.

II. Request for the Clarification of the Status of Claim 33

Claim 33 was cancelled in Response C, yet the Examiner has counted it as a pending claim. Applicants respectfully request that the Examiner update her records to indicate the cancellation of claim 33.

III. Discussion of the Request to Withdraw Finality

A Request For Withdrawal of Premature Final Rejection under MPEP Sec. 706.07(c-d) accompanies this response. Applicants do believe that the finality of the previous Office Action was premature. Applicants continue to assert that they are entitled to the benefit of priority from the original Japanese patent application, thus obviating the art rejections.

However, in addition to their insistence on the appropriateness of priority as delineated in Sec. XIII on page 30 of Response C, they also provided scientific bases for non-obviousness of the amended claims in Secs. X and XI on pages 25 and 26 of Response C. Unfortunately, the Examiner only addressed the issue of the priority benefit, and provided no comment on the other arguments for non-obviousness. Accordingly, Applicants hereby respectfully request the Examiner's consideration of the arguments made on pages 25 and 26 of Response C filed June 18, 2004. In addition, further comments are made in the present response to supplement the previous arguments in light of the Final Office Action.

IV. Discussion of the 35 U.S.C. Sec. 103(a) Rejection over Kato *et al.*

Claims 1, 2, 5, 7, 8, 11-16, 25-29, 32-36 and 38-41 have been rejected under 35 U.S.C. Sec. 103(a) as being unpatentable over Kato *et al.*, (CA 134:266103 (2001)). Applicants respectfully traverse the rejection.

As an initial matter, Applicants note that all of the pending claims but claim 9 were listed as rejected over the cited reference. Applicants respectfully request clarification as to whether or not claim 9 is free of the cited art. In addition, claim 33 is listed as rejected, even though it was previously cancelled.

The Examiner has cited compound 331756-17-3 and Example 202 in her discussion of Kato *et al.* Applicants wish to point out to the Examiner that the central linking group in both of the specifically-mentioned compounds is an aryl unit. That central linking unit holds the same position in the molecule as variable E in general formula I of independent claim 1 as amended. E has previously been limited to a trimethylene group. Therefore, the middle portion of compounds of the present claim 1 is non-aromatic, while the middle portion of compounds of the cited art is aromatic. Thus, the presently claimed compounds are non-obvious non-homologues of the compounds in the cited art.

Moreover, the Examiner's comments about R² being a methyl group are confusing. In Applicants' claimed compounds, R² is not methyl. Applicants respectfully request that the Examiner consider the cited art in light of the pending claims, focusing on the differences imparted by variable E. The differences are non-obvious.

Claims 2, 5, 7, 8, 11-13, 15, 16, 25, 28, 29, 32, 34-36 and 38-41 depend upon claim 1. Applicants submit that the more specific dependent claims are also non-obvious for the reason provided above.

Claim 14 is an independent claim, directed to specific compounds. The Examiner is requested to indicate how these specific compounds are obvious over the cited art, as Applicants assert that they are structurally different and therefore non-obvious. Applicants respectfully request that the Examiner refer to Appendix A of the response filed June 18, 2004, wherein the structures of the compounds recited in claim 14 were previously provided for the Examiner's convenience. Examples 23, 51, 76, 84 and 93 in the Appendix are the first through fifth compounds respectively in claim 14.

Claim 26 is an independent method claim directed to the production of compounds of general formula (I). Claim 26 was previously amended to recite that E is a trimethylene group. Applicants assert that the same reasoning described above with respect to independent claim 1 may also be applied to claim 26, rendering it also non-obvious in light of the cited art.

Claim 27 is an independent method claim directed to the production of compounds of general formula (I). Claim 27 was previously amended to recite that E is a trimethylene group. Applicants assert that the same reasoning described above with respect to independent claim 1 may also be applied to claim 27, rendering it also non-obvious in light of the cited art.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) rejection over Kato *et al.*

V. Discussion of the 35 U.S.C. Sec. 103(a) Rejection over Kim *et al.* in view of Caldwell *et al.*

Claims 1, 2, 5, 7, 8, 11-16, 25-29, 32-36 and 38-41 have been rejected under 35 U.S.C. Sec. 103(a) as being unpatentable over Kim *et al.* (U.S. Patent 6,511,994) in view of Caldwell *et al.* (U.S. Patent 6,136,827). Applicants respectfully traverse the rejection.

As an initial matter, Applicants note that all of the pending claims but claim 9 were listed as rejected over the cited reference. Applicants respectfully request clarification as to whether or not claim 9 is free of the cited art. In addition, claim 33 is listed as rejected, even though it was previously cancelled.

In the Final Office Action, the Examiner merely copied her previous rejection of April 18, 2003, without adding any comments pertinent to the pending claims as amended. Applicants can only assume by the lack of pertinent comments that their carefully crafted explanations were not even read. For this reason, the arguments previously made are now re-presented.

Applicants would like to request that the Examiner consider the non-obviousness of the pending claims over the combined teachings of the cited art in light of the identity of variable E and the following arguments.

The Examiner has specifically noted Example 42 as a relevant compound in Kim *et al.* In that compound, the amide nitrogen is unsubstituted and the portion near the center of the molecule is a phenyl-substituted trimethylene group. By contrast, the compounds set forth in claim 1 as previously amended have a substituted amide nitrogen (R³) and the portion near the center of the molecule (E) is an unsubstituted trimethylene group. In cols. 4 and 104 of the cited reference, compounds of general formula (I) are defined as having R⁴ as phenyl, naphthyl or heterocyclyl groups, meaning that the trimethylene group is always substituted.

The Examiner believes that since Caldwell *et al.* teach compounds having amide functionality wherein nitrogen may be substituted, one skilled in the art could combine the teachings of Kim *et al.* with the teachings of Caldwell *et al.*, to obtain the presently claimed compounds.

However, Applicants assert that were one skilled in the art to combine the teachings of the two references, the combined teaching of the cited references would actually *teach away* from the aspects of Applicants' invention set forth in independent claim 1 as previously amended. This is so because Applicants' E group is identified as a trimethylene group, whereas the cited art teaches that an equivalent linking group should have an aryl substituent.

More specifically, the Examiner has cited the numerous example compounds found in cols. 16 – 61 of Caldwell *et al.* in a previous Office Action. Yet none of the two hundred and fifty three compounds exemplified in that reference have an unsubstituted trimethylene group. Moreover, in Kim *et al.*, none of the seventy-eight synthetic examples have an unsubstituted trimethylene group. So one skilled in the art reviewing these two references might well assume that substitution on the trimethylene group is essential. This would teach away from Applicants' invention as set forth in independent claim 1 as previously amended.

Claims 2, 5, 7, 8, 11-13, 15, 16, 25-29, 32, 34-36 and 38-41 depend upon claim 1. Applicants submit that the more specific dependent claims are also non-obvious for the reason provided above.

Claim 14 is an independent claim, directed to specific compounds. The Examiner is requested to indicate how these specific compounds are obvious over the combined teachings of the cited art, as Applicants assert that they are structurally different and therefore non-obvious. Applicants respectfully request that the Examiner refer to Appendix A of the response filed June 18, 2004, wherein the structures of the compounds recited in claim 14 were previously provided for the Examiner's convenience. Examples 23, 51, 76, 84 and 93 in the Appendix are the first through fifth compounds respectively in claim 14.

Claim 26 is an independent method claim directed to the production of compounds of general formula (I). Claim 26 was previously amended to recite that E is a trimethylene group. Applicants assert that the same reasoning described above with respect to independent claim 1 may also be applied to claim 26, rendering it also non-obvious in light of the combined teachings of the cited art.

Claim 27 is an independent method claim directed to the production of compounds of general formula (I). Claim 27 was previously amended to recite that E is a trimethylene group. Applicants assert that the same reasoning described above with respect to independent claim 1 may also be applied to claim 27, rendering it also non-obvious in light of the combined teachings of the cited art.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) rejection over Kim *et al.* in view of Caldwell *et al.*

VI. Discussion of the 35 U.S.C. Sec. 103(a) Rejection over Weber *et al.* in view of Chepkova *et al.* and Patani *et al.*

Claims 1-16 and 30-39 under 35 U.S.C. Sec. 103(a) had previously been rejected as allegedly obvious over Weber *et al.*, U.S. Patent No. 4,891,378 in view of Chepkova *et al.*, Chem Abs. 1991:157055 and Patani *et al.* in Chem. Rev. 1996, 96, 3147-3176.

However, this rejection was not discussed in the Final Office Action dated September 16, 2004. Applicants respectfully request that the Examiner indicate for the record whether this rejection has been maintained or overcome.

VII. Discussion of the Denial of the Benefit of Priority from the Parent Japanese Patent Application

The Examiner has adamantly maintained her position that the benefit of priority from the parent Japanese patent application should be denied.

However, Applicants painstakingly demonstrated in great detail in Response C that the aspects of their invention as set forth in pending *claims* all can be found in the priority document, by specifically citing the location of the basis for *each claim* in the certified copy of the translation of the priority document. The Examiner has yet to refute this evidence. Applicants respectfully request that the Examiner carefully review the detailed information provided on pages 30- 42 of Response C.

Rather than address the content of the claims, the Examiner has continued only to copy over her previous comments from earlier Actions. Unfortunately these comments only illustrate that the Examiner will not accord Applicants the priority which they are entitled to because she has found portions of the priority document which do not read exactly the same as the present specification. Yet the comments do not address whether or not *the language of the pending claims* is supported by the priority document.

Applicants respectfully request that the Examiner simply consider claim 1. Is it, or is it not supported by the language in the priority document? If the Examiner finds that it is not, Applicants respectfully request that the Examiner indicate for the record what aspects of pending claim 1 are not found in the priority document. The rest of the claims should be analyzed in a similar manner.

Upon so doing, the Examiner should find that a claim of the benefit of priority is indeed proper.

VIII. Discussion of the Objection to the Previous Amendment of the Disclosure

The Examiner has objected to the previous amendments to the disclosure at pages 9, 14 and 17 for allegedly containing new matter. Applicants disagree that the amendments add new matter, but to expedite prosecution the objected to previously added matter has been deleted from the specification.

Therefore Applicants respectfully request withdrawal of the objection to the disclosure.

IX. Discussion of the Rejection of the Claims under 35 U.S.C. Sec. 112, First Paragraph

The Examiner has indicated on the bottom of page 3 of the Office Action, that the claims have been rejected under 35 U.S.C. Sec. 112, first paragraph as containing new matter.

Applicants do not believe that the claims contain any new matter, and therefore respectfully request withdrawal of the 35 U.S.C. Sec. 112, first paragraph rejection of the claims.

Should the Examiner continue to maintain the rejection, Applicants respectfully request that the Examiner specifically point out exactly what language in each claim she finds to be new matter, to avoid making prosecution unduly prolix.

X. Discussion of the 35 U.S.C. Sec. 112, Second Paragraph Rejection of Claim 1

The rejection of claim 1 under 35 U.S.C. Sec. 112, second paragraph for the ambiguity or hydrocarbon moiety containing non-carbon or hydrogen structure has been maintained. Applicants respectfully traverse this rejection.

As the Applicants have previously explained, their specification teaches that hydrocarbon groups can have optional substituents. The optional substituents of the hydrocarbon groups can be heterocyclic. It is evident that the Examiner is confused by this, but Applicants believe that the standard is whether or not one skilled in the art of organic synthesis could understand the claim based on their knowledge of the art and the teachings of the specification; not whether or not the claim is confusing to the Examiner. Applicants assert that what is claimed in claim 1 is unambiguous to those skilled in the art.

Chemists may choose to define substituents of hydrocarbon groups to include heterocycles, as Applicants have done in the present application. Though the Examiner seems to be confused by this point now, in other patents which she examined, it was apparently not so confusing.

As has been stated before, the Examiner has examined and allowed patents including claims reciting hydrocarbon groups which are optionally substituted, wherein the optional substituents may be heterocyclic. See U.S. Patent No. 6,548,674 for example.

What is not confusing are the pending claims. What is confusing is the unequal treatment of the examination of the present claims in comparison to other cases which the same Examiner has handled.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, second paragraph rejection of claim 1.

XI. Discussion of the 35 U.S.C. Sec. 112, Second Paragraph Rejection of Claim 16

Claim 16 has been rejected under 35 U.S.C. Sec. 112, second paragraph as allegedly self-conflicting. Applicants respectfully traverse this rejection.

To expedite prosecution, Applicants have amended claim 16 in the manner which the Examiner has suggested. Support for the amendment may be found in the specification at page 37, lines 15-32 *inter alia*.

Therefore, Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, second paragraph rejection of claim 16.

XII. Discussion of the 35 U.S.C. Sec. 112, First Paragraph Rejection of Claim 15

The rejection of claim 15 under 35 U.S.C. Sec. 112, first paragraph as allegedly not enabled as to the term “pro-drug” has been maintained. Applicants respectfully traverse the rejection.

To expedite prosecution, Applicants have amended claim 15 to limit the claim to the scope which the Examiner has suggested. This amendment adds no new matter to the specification. Support for the amendment may be found in the specification at page 26, lines 12-33 *inter alia*.

Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, first paragraph rejection of claim 15.

XIII. Discussion of the 35 U.S.C. Sec. 112, First Paragraph Rejection of Claim 28

The rejection of claim 28 under 35 U.S.C. Sec. 112, first paragraph as allegedly not enabled has been maintained.

By this amendment, Applicants have amended claim 28 to the aspects of the invention which the Examiner has already found to be enabled to expedite prosecution. This amendment adds no new matter to the specification. Support for the amendment may be found in the specification at page 2, lines 21-29 *inter alia*.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, first paragraph rejection of claim 28.

XIV. Conclusion

Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, she is respectfully invited to call Applicants' attorney at the number below.

Respectfully submitted,

Dated: January 14, 2005

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